```
  * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:55:08 ON 04 OCT 2002

=> fil .bec,canc
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILES 'MEDLINE, SCISEARCH, LIFESCI, BIOTECHDS, BIOSIS, EMBASE, HCAPLUS, NTIS,
       ESBIOBASE, BIOTECHNO, WPIDS, CANCERLIT' ENTERED AT 10:55:40 ON 04 OCT 2002
ALL COPYRIGHTS AND RESTRICTIONS APPLY.  SEE HELP USAGETERMS FOR DETAILS.

12 FILES IN THE FILE LIST

=> s hbx
FILE 'MEDLINE'
L1          271 HBX

FILE 'SCISEARCH'
L2          333 HBX

FILE 'LIFESCI'
L3          173 HBX

FILE 'BIOTECHDS'
L4            8 HBX

FILE 'BIOSIS'
L5          303 HBX

FILE 'EMBASE'
L6          235 HBX

FILE 'HCAPLUS'
L7          571 HBX

FILE 'NTIS'
L8           26 HBX

FILE 'ESBIOBASE'
L9          162 HBX

FILE 'BIOTECHNO'
L10         188 HBX

FILE 'WPIDS'
L11          11 HBX

FILE 'CANCERLIT'
L12         184 HBX

TOTAL FOR ALL FILES
L13        2465 HBX

=> s (hepatitis b virus or hbv)(8a)(inhibit? or treat?)
FILE 'MEDLINE'
         109521 HEPATITIS
         514868 B
         335961 VIRUS
          17542 HEPATITIS B VIRUS
                  (HEPATITIS(W)B(W)VIRUS)
          10383 HBV
         985513 INHIBIT?
```

```
       1781455 TREAT?
L14       1613 (HEPATITIS B VIRUS OR HBV)(8A)(INHIBIT? OR TREAT?)

FILE 'SCISEARCH'
         77462 HEPATITIS
        917642 B
        286160 VIRUS
         13297 HEPATITIS B VIRUS
                 (HEPATITIS(W)B(W)VIRUS)
          8576 HBV
        773789 INHIBIT?
       1295460 TREAT?
L15       1450 (HEPATITIS B VIRUS OR HBV)(8A)(INHIBIT? OR TREAT?)

FILE 'LIFESCI'
         19514 "HEPATITIS"
        175323 "B"
        166689 "VIRUS"
          7964 HEPATITIS B VIRUS
                 ("HEPATITIS"(W)"B"(W)"VIRUS")
          4061 HBV
        274168 INHIBIT?
        272165 TREAT?
L16        611 (HEPATITIS B VIRUS OR HBV)(8A)(INHIBIT? OR TREAT?)

FILE 'BIOTECHDS'
          3291 HEPATITIS
         33567 B
         34653 VIRUS
          1666 HEPATITIS B VIRUS
                 (HEPATITIS(W)B(W)VIRUS)
           424 HBV
         36341 INHIBIT?
         56196 TREAT?
L17        107 (HEPATITIS B VIRUS OR HBV)(8A)(INHIBIT? OR TREAT?)

FILE 'BIOSIS'
         93067 HEPATITIS
        610835 B
        451986 VIRUS
         22934 HEPATITIS B VIRUS
                 (HEPATITIS(W)B(W)VIRUS)
         10708 HBV
       1071051 INHIBIT?
       1563208 TREAT?
L18       1719 (HEPATITIS B VIRUS OR HBV)(8A)(INHIBIT? OR TREAT?)

FILE 'EMBASE'
         82054 "HEPATITIS"
        540843 "B"
        363355 "VIRUS"
         17830 HEPATITIS B VIRUS
                 ("HEPATITIS"(W)"B"(W)"VIRUS")
          8860 HBV
        880153 INHIBIT?
       1686240 TREAT?
L19       1540 (HEPATITIS B VIRUS OR HBV)(8A)(INHIBIT? OR TREAT?)

FILE 'HCAPLUS'
         35675 HEPATITIS
       1303216 B
        272912 VIRUS
          9076 HEPATITIS B VIRUS
                 (HEPATITIS(W)B(W)VIRUS)
```

```
          5198 HBV
       1515605 INHIBIT?
       2794759 TREAT?
L20       1405 (HEPATITIS B VIRUS OR HBV)(8A)(INHIBIT? OR TREAT?)

FILE 'NTIS'
          1190 HEPATITIS
         65064 B
          7228 VIRUS
           122 HEPATITIS B VIRUS
                 (HEPATITIS(W)B(W)VIRUS)
            80 HBV
         19479 INHIBIT?
        117746 TREAT?
L21          6 (HEPATITIS B VIRUS OR HBV)(8A)(INHIBIT? OR TREAT?)

FILE 'ESBIOBASE'
         16571 HEPATITIS
        216552 B
         74643 VIRUS
          3646 HEPATITIS B VIRUS
                 (HEPATITIS(W)B(W)VIRUS)
          2913 HBV
        302510 INHIBIT?
        375533 TREAT?
L22        542 (HEPATITIS B VIRUS OR HBV)(8A)(INHIBIT? OR TREAT?)

FILE 'BIOTECHNO'
         24280 HEPATITIS
        197094 B
        161273 VIRUS
          7508 HEPATITIS B VIRUS
                 (HEPATITIS(W)B(W)VIRUS)
          4475 HBV
        266821 INHIBIT?
        247727 TREAT?
L23        812 (HEPATITIS B VIRUS OR HBV)(8A)(INHIBIT? OR TREAT?)

FILE 'WPIDS'
          8448 HEPATITIS
       1006577 B
         28121 VIRUS
          1102 HEPATITIS B VIRUS
                 (HEPATITIS(W)B(W)VIRUS)
           599 HBV
        183570 INHIBIT?
        790621 TREAT?
L24        314 (HEPATITIS B VIRUS OR HBV)(8A)(INHIBIT? OR TREAT?)

FILE 'CANCERLIT'
         21297 HEPATITIS
        138100 B
        120237 VIRUS
          5215 HEPATITIS B VIRUS
                 (HEPATITIS(W)B(W)VIRUS)
          3459 HBV
        236011 INHIBIT?
        510057 TREAT?
L25        809 (HEPATITIS B VIRUS OR HBV)(8A)(INHIBIT? OR TREAT?)

TOTAL FOR ALL FILES
L26      10928 (HEPATITIS B VIRUS OR HBV)(8A)(INHIBIT? OR TREAT?)

=> s l13 and l26
```

```
FILE 'MEDLINE'
L27          22 L1 AND L14

FILE 'SCISEARCH'
L28          23 L2 AND L15

FILE 'LIFESCI'
L29          15 L3 AND L16

FILE 'BIOTECHDS'
L30           1 L4 AND L17

FILE 'BIOSIS'
L31          25 L5 AND L18

FILE 'EMBASE'
L32          20 L6 AND L19

FILE 'HCAPLUS'
L33          67 L7 AND L20

FILE 'NTIS'
L34           0 L8 AND L21

FILE 'ESBIOBASE'
L35          19 L9 AND L22

FILE 'BIOTECHNO'
L36          16 L10 AND L23

FILE 'WPIDS'
L37           2 L11 AND L24

FILE 'CANCERLIT'
L38          19 L12 AND L25

TOTAL FOR ALL FILES
L39         229 L13 AND L26

=> s l13(10a)inhibit?
FILE 'MEDLINE'
        985513 INHIBIT?
L40          48 L1 (10A)INHIBIT?

FILE 'SCISEARCH'
        773789 INHIBIT?
L41          42 L2 (10A)INHIBIT?

FILE 'LIFESCI'
        274168 INHIBIT?
L42          38 L3 (10A)INHIBIT?

FILE 'BIOTECHDS'
         36341 INHIBIT?
L43           1 L4 (10A)INHIBIT?

FILE 'BIOSIS'
       1071051 INHIBIT?
L44          45 L5 (10A)INHIBIT?

FILE 'EMBASE'
        880153 INHIBIT?
L45          41 L6 (10A)INHIBIT?
```

```
FILE 'HCAPLUS'
      1515605 INHIBIT?
L46         59 L7 (10A)INHIBIT?

FILE 'NTIS'
        19479 INHIBIT?
L47          0 L8 (10A)INHIBIT?

FILE 'ESBIOBASE'
       302510 INHIBIT?
L48         36 L9 (10A)INHIBIT?

FILE 'BIOTECHNO'
       266821 INHIBIT?
L49         36 L10(10A)INHIBIT?

FILE 'WPIDS'
       183570 INHIBIT?
L50          2 L11(10A)INHIBIT?

FILE 'CANCERLIT'
       236011 INHIBIT?
L51         44 L12(10A)INHIBIT?

TOTAL FOR ALL FILES
L52        392 L13(10A) INHIBIT?

=> s (139 or l52) not 1998-2002/py
FILE 'MEDLINE'
      2240127 1998-2002/PY
L53         17 (L27 OR L40) NOT 1998-2002/PY

FILE 'SCISEARCH'
      4507425 1998-2002/PY
L54         13 (L28 OR L41) NOT 1998-2002/PY

FILE 'LIFESCI'
       471204 1998-2002/PY
L55         12 (L29 OR L42) NOT 1998-2002/PY

FILE 'BIOTECHDS'
        66968 1998-2002/PY
L56          1 (L30 OR L43) NOT 1998-2002/PY

FILE 'BIOSIS'
      2507478 1998-2002/PY
L57         15 (L31 OR L44) NOT 1998-2002/PY

FILE 'EMBASE'
      2014215 1998-2002/PY
L58         14 (L32 OR L45) NOT 1998-2002/PY

FILE 'HCAPLUS'
      4217175 1998-2002/PY
L59         31 (L33 OR L46) NOT 1998-2002/PY

FILE 'NTIS'
        91857 1998-2002/PY
L60          0 (L34 OR L47) NOT 1998-2002/PY

FILE 'ESBIOBASE'
      1314709 1998-2002/PY
L61          9 (L35 OR L48) NOT 1998-2002/PY
```

```
FILE 'BIOTECHNO'
       547247 1998-2002/PY
L62         13 (L36 OR L49) NOT 1998-2002/PY

FILE 'WPIDS'
      3616741 1998-2002/PY
L63          0 (L37 OR L50) NOT 1998-2002/PY

FILE 'CANCERLIT'
       420563 1998-2002/PY
L64         19 (L38 OR L51) NOT 1998-2002/PY

TOTAL FOR ALL FILES
L65        144 (L39 OR L52) NOT 1998-2002/PY

=> dup rem l65
PROCESSING COMPLETED FOR L65
L66          37 DUP REM L65 (107 DUPLICATES REMOVED)

=> d tot

L66  ANSWER 1 OF 37  HCAPLUS  COPYRIGHT 2002 ACS
TI   Ribozymes directed against hepatitis B virus
     RNA and the treatment of viral infection
SO   PCT Int. Appl., 34 pp.
     CODEN: PIXXD2
IN   Goldenberg, Tsvi; Yu, Mang; Welch, Peter J.; Barber, Jack R.
AN   1997:244380  HCAPLUS
DN   126:220698
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 9708309         A2   19970306      WO 1996-US13975  19960829
     WO 9708309         A3   19970710
          W:  CA, JP
          RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

L66  ANSWER 2 OF 37     MEDLINE                          DUPLICATE 1
TI   Activating transcription factor 2 (ATF2) down-regulates hepatitis B virus
     X promoter activity by the competition for the activating protein 1
     binding site and the formation of the ATF2-Jun heterodimer.
SO   JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Jul 4) 272 (27) 16934-9.
     Journal code: 2985121R. ISSN: 0021-9258.
AU   Choi C Y; Choi B H; Park G T; Rho H M
AN   97347498     MEDLINE

L66  ANSWER 3 OF 37     MEDLINE                          DUPLICATE 2
TI   Hepatitis B virus X protein and p53 tumor suppressor interactions in the
     modulation of apoptosis.
SO   PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF
     AMERICA, (1997 Dec 23) 94 (26) 14707-12.
     Journal code: 7505876. ISSN: 0027-8424.
AU   Elmore L W; Hancock A R; Chang S F; Wang X W; Chang S; Callahan C P;
     Geller D A; Will H; Harris C C
AN   1998070816     MEDLINE

L66  ANSWER 4 OF 37     MEDLINE                          DUPLICATE 3
TI   Hepatitis B virus HBx protein sensitizes cells to apoptotic killing by
     tumor necrosis factor alpha.
SO   PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF
     AMERICA, (1997 Aug 5) 94 (16) 8744-9.
     Journal code: 7505876. ISSN: 0027-8424.
AU   Su F; Schneider R J
AN   97385174     MEDLINE
```

L66 ANSWER 5 OF 37 MEDLINE DUPLICATE 4
TI The transactivation and p53-interacting functions of hepatitis B virus X protein are mutually interfering but distinct.
SO CANCER RESEARCH, (1997 Nov 15) 57 (22) 5137-42.
Journal code: 2984705R. ISSN: 0008-5472.
AU Lin Y; Nomura T; Yamashita T; Dorjsuren D; Tang H; Murakami S
AN 1998037566 MEDLINE

L66 ANSWER 6 OF 37 MEDLINE DUPLICATE 5
TI **Inhibition** of hepatocellular carcinoma development in **hepatitis B virus** transfected mice by low dietary casein.
SO HEPATOLOGY, (1997 Nov) 26 (5) 1351-4.
Journal code: 8302946. ISSN: 0270-9139.
AU Cheng Z; Hu J; King J; Jay G; Campbell T C
AN 1998026706 MEDLINE

L66 ANSWER 7 OF 37 CANCERLIT
TI The carboxyl terminal domain of hepatitis B virus X protein binds to p53 and abrogates p53-mediated apoptosis (Meeting abstract).
SO Proc Annu Meet Am Assoc Cancer Res, (1997) 38 A1137.
ISSN: 0197-016X.
AU Elmore L; Hancock A; Callahan C; Will H; Chang S-F; Wang X; Harris C
AN 1998638137 CANCERLIT

L66 ANSWER 8 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI XAP2, a novel **hepatitis B virus** X-associated protein that **inhibits** X transactivation
SO Nucleic Acids Research (1996), 24(23), 4741-4750
CODEN: NARHAD; ISSN: 0305-1048
AU Kuzhandaivelu, Nadarajan; Cong, Yu-Sheng; Inouye, Carla; Yang, Wen-Ming; Seto, Edward
AN 1997:6596 HCAPLUS
DN 126:55707

L66 ANSWER 9 OF 37 MEDLINE DUPLICATE 6
TI Hepatitis B virus HBx protein activates transcription factor NF-kappaB by acting on multiple cytoplasmic inhibitors of rel-related proteins.
SO JOURNAL OF VIROLOGY, (1996 Jul) 70 (7) 4558-66.
Journal code: 0113724. ISSN: 0022-538X.
AU Su F; Schneider R J
AN 96256768 MEDLINE

L66 ANSWER 10 OF 37 CANCERLIT
TI Human cytomegalovirus immediate-early protein IE2 transmodulates hepatitis B virus gene expression: implications of synergism in hepatocarcinogenesis (Meeting abstract).
SO Proc Annu Meet Am Assoc Cancer Res, (1996) 37 A3865.
ISSN: 0197-016X.
AU Chen S-C; Wu FY-H; Wu C-W
AN 96709767 CANCERLIT

L66 ANSWER 11 OF 37 MEDLINE DUPLICATE 7
TI **Inhibition** of **hepatitis-B-virus** core promoter by p53: implications for carcinogenesis in hepatocytes.
SO INTERNATIONAL JOURNAL OF CANCER, (1996 Sep 17) 67 (6) 892-7.
Journal code: 0042124. ISSN: 0020-7136.
AU Uchida T; Takahashi K; Tatsuno K; Dhingra U; Eliason J F
AN 96421947 MEDLINE

L66 ANSWER 12 OF 37 MEDLINE DUPLICATE 8
TI The effect of **hepatitis B virus** X gene expression on response to growth **inhibition** by transforming growth factor-beta 1.

SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1996 May 24) 222 (3) 770-3.
Journal code: 0372516. ISSN: 0006-291X.
AU Oshikawa O; Tamura S; Kawata S; Ito N; Tsushima H; Kiso S; Matsuda Y; Yamada A; Tamai S; Matsuzawa Y
AN 96244576 MEDLINE

L66 ANSWER 13 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI Hepatitis B virus pX activates NF-.kappa.B-dependent transcription through a Raf-independent pathway
SO Journal of Virology (1996), 70(1), 641-6
CODEN: JOVIAM; ISSN: 0022-538X
AU Chirillo, Paolo; Falco, Mirella; Puri, Pier Lorenzo; Artini, Marco; Balsano, Clara; Levrero, Massimo; Natoli, Gioacchino
AN 1995:990553 HCAPLUS
DN 124:52376

L66 ANSWER 14 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI Application of radiolabeled anti-HBx monoclonal antibody for HCC targeting therapy
SO Zhonghua Yixue Zazhi (1996), 76(4), 271-274
CODEN: CHHTAT; ISSN: 0376-2491
AU Li, Jun; Tang, Zhaoyou; Liu, Kangda; Dai, Zhunyan
AN 1996:589513 HCAPLUS
DN 125:241865

L66 ANSWER 15 OF 37 MEDLINE DUPLICATE 9
TI In vivo **inhibition** of **hepatitis B virus** gene expression by antisense phosphorothioate oligonucleotides.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1996 Jan 5) 218 (1) 217-23.
Journal code: 0372516. ISSN: 0006-291X.
AU Moriya K; Matsukura M; Kurokawa K; Koike K
AN 96136303 MEDLINE

L66 ANSWER 16 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI Antiviral and anti-proliferative activities of .alpha. interferons in experimental hepatitis B virus infections
SO Antiviral Therapy (1996), 1(Suppl. 4, Therapies for Viral Hepatitis), 64-70
CODEN: ANTHFA; ISSN: 1359-6535
AU Gangemi, J. David; Korba, Brent; Tennant, Bud; Ueda, Hiroyuki; Jay, Gilbert
AN 1997:228421 HCAPLUS
DN 126:262824

L66 ANSWER 17 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI Hepatitis B virus (HBV) interacts with cellular DNA repair processes
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
IN Butel, Janet S.; Lee, Teh-Hsiu; Elledge, Stephen J.
AN 1995:761653 HCAPLUS
DN 123:311748

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9510288	A1	19950420	WO 1994-US11451	19941012
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9479725	A1	19950504	AU 1994-79725	19941012

L66 ANSWER 18 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI X-gene product antagonizes the p53-mediated **inhibition** of **hepatitis B virus** replication through

regulation of the pregenomic/core promoter
SO Journal of Biological Chemistry (1995), 270(52), 31405-12
CODEN: JBCHA3; ISSN: 0021-9258
AU Lee, Hyunsook; Lee, Young-Ho; Huh, Yun-Sil; Moon, Hongmo; Yun, Yungdae
AN 1996:29140 HCAPLUS
DN 124:108778

L66 ANSWER 19 OF 37 MEDLINE DUPLICATE 10
TI Abrogation of p53-induced apoptosis by the hepatitis B virus X gene.
SO CANCER RESEARCH, (1995 Dec 15) 55 (24) 6012-6.
Journal code: 2984705R. ISSN: 0008-5472.
AU Wang X W; Gibson M K; Vermeulen W; Yeh H; Forrester K; Sturzbecher H W; Hoeijmakers J H; Harris C C
AN 96105011 MEDLINE

L66 ANSWER 20 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI Expression of the terminal protein region of **hepatitis B virus inhibits** cellular responses to interferons .alpha. and .gamma. and double-stranded RNA. [Erratum to document cited in CA114:205330]
SO Proceedings of the National Academy of Sciences of the United States of America (1995), 92(8), 3632
CODEN: PNASA6; ISSN: 0027-8424
AU Foster, Graham R.; Ackrill, Andrew M.; Goldin, Robert D.; Kerr, Ian M.; Thomas, Howard C.; Stark, George R.
AN 1995:510542 HCAPLUS
DN 123:7696

L66 ANSWER 21 OF 37 MEDLINE DUPLICATE 11
TI Direct interaction of the **hepatitis B virus HBx** protein with p53 leads to **inhibition** by **HBx** of p53 response element-directed transactivation.
SO JOURNAL OF VIROLOGY, (1995 Mar) 69 (3) 1851-9.
Journal code: 0113724. ISSN: 0022-538X.
AU Truant R; Antunovic J; Greenblatt J; Prives C; Cromlish J A
AN 95156618 MEDLINE

L66 ANSWER 22 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI Disruption of the function of tumor-suppressor gene p53 by the hepatitis B virus X protein and hepatocarcinogenesis
SO Journal of Cancer Research and Clinical Oncology (1995), 121(9/10), 593-601
CODEN: JCROD7; ISSN: 0171-5216
AU Takada, Shinako; Tsuchida, Nobuo; Kobayashi, Midori; Koike, Katsuro
AN 1996:4128 HCAPLUS
DN 124:83486

L66 ANSWER 23 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI Putative secondary structure of human hepatitis B viral X mRNA
SO Journal of Biochemistry and Molecular Biology (1995), 28(6), 509-14
CODEN: JBMBE5; ISSN: 1225-8687
AU Kim, Hadong; Choi, Yoon Chul; Lee, Bum Yong; Junn, Eunsung; Ahn, Jeongkeun; Kang, Changwon; Park, Inwon
AN 1995:1007863 HCAPLUS
DN 124:110002

L66 ANSWER 24 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI **Inhibition** of **hepatitis B virus** X protein gene expression by its antisense RNA in E. coli
SO Wuhan Daxue Xuebao, Ziran Kexueban (1995), 41(4), 475-81
CODEN: WTHPDI; ISSN: 0253-9888
AU Yang, Jianqi; Zhang, Xiyuan; Li, Wenxin; Zhang, Xiaogang; Wang, Ping
AN 1996:60066 HCAPLUS
DN 124:137017

L66 ANSWER 25 OF 37 MEDLINE DUPLICATE 12
TI **Inhibition** of **HBx** gene expression by antisense oligonucleotide.
SO NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (1995 Oct) 53 Suppl 111-4. Ref: 9
Journal code: 0420546. ISSN: 0047-1852.
AU Moriya K; Koike K
AN 96060243 MEDLINE

L66 ANSWER 26 OF 37 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
TI Functional inactivation but not structural mutation of p53 causes liver cancer;
hepatitis B virus gene expression in transgenic mouse, application as a liver tumor disease model
SO Nat.Genet.; (1995) 9, 1, 41-47
CODEN: 6906K
AU Ueda H; Ullrich S J; Gangemi J D; Kappel C A; Ngo L; Feitelson M A; *Jay G
AN 1995-02158 BIOTECHDS

L66 ANSWER 27 OF 37 MEDLINE DUPLICATE 13
TI Hepatitis B virus HBx protein activates Ras-GTP complex formation and establishes a Ras, Raf, MAP kinase signaling cascade.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Oct 25) 91 (22) 10350-4.
Journal code: 7505876. ISSN: 0027-8424.
AU Benn J; Schneider R J
AN 95024111 MEDLINE

L66 ANSWER 28 OF 37 MEDLINE DUPLICATE 14
TI **Hepatitis B virus** X protein **inhibits** p53 sequence-specific DNA binding, transcriptional activity, and association with transcription factor ERCC3.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Mar 15) 91 (6) 2230-4.
Journal code: 7505876. ISSN: 0027-8424.
AU Wang X W; Forrester K; Yeh H; Feitelson M A; Gu J R; Harris C C
AN 94181566 MEDLINE

L66 ANSWER 29 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI Interaction of hepatitis B virus X protein with a serine protease, tryptase TL2 as an inhibitor
SO Oncogene (1994), 9(2), 341-8
CODEN: ONCNES; ISSN: 0950-9232
AU Takada, Shinako; Kido, Hiroshi; Fukutomi, Aiko; Mori, Takeshi; Koike, Katsuro
AN 1994:211292 HCAPLUS
DN 120:211292

L66 ANSWER 30 OF 37 MEDLINE DUPLICATE 15
TI Transactivation of human hepatitis B virus X protein, HBx, operates through a mechanism distinct from protein kinase C and okadaic acid activation pathways.
SO VIROLOGY, (1994 Feb 15) 199 (1) 243-6.
Journal code: 0110674. ISSN: 0042-6822.
AU Murakami S; Cheong J; Ohno S; Matsushima K; Kaneko S
AN 94160577 MEDLINE

L66 ANSWER 31 OF 37 CANCERLIT
TI Interaction of human hepatitis B virus X protein and p53 (Meeting abstract).
SO Proc Annu Meet Jpn Cancer Assoc, (1994) 6 145.
ISSN: 0546-0476.

AU Lin Y; Cheong J; Murakami S
AN 96600534 CANCERLIT

L66 ANSWER 32 OF 37 MEDLINE DUPLICATE 16
TI The hepatitis B virus transactivator HBx causes elevation of diacylglycerol and activation of protein kinase C.
SO RESEARCH IN VIROLOGY, (1993 Jul-Aug) 144 (4) 311-21.
Journal code: 8907469. ISSN: 0923-2516.
AU Luber B; Lauer U; Weiss L; Hohne M; Hofschneider P H; Kekule A S
AN 94023459 MEDLINE

L66 ANSWER 33 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI Methods for using recombinant bacteria to identify and produce medically important agents
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
IN Block, Timothy M.; Grafstrom, Robert H.
AN 1993:206927 HCAPLUS
DN 118:206927

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9213972	A1	19920820	WO 1992-US1188	19920211
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
US 5532124	A	19960702	US 1993-98313	19931006

L66 ANSWER 34 OF 37 MEDLINE DUPLICATE 17
TI **Hepatitis B virus** transactivator MHBst: activation of NF-kappa B, selective **inhibition** by antioxidants and integral membrane localization.
SO EMBO JOURNAL, (1992 Aug) 11 (8) 2991-3001.
Journal code: 8208664. ISSN: 0261-4189.
AU Meyer M; Caselmann W H; Schluter V; Schreck R; Hofschneider P H; Baeuerle P A
AN 92347334 MEDLINE

L66 ANSWER 35 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI Expression of the terminal protein region of **hepatitis B virus inhibits** cellular responses to interferons .alpha. and .gamma. and double-stranded RNA
SO Proc. Natl. Acad. Sci. U. S. A. (1991), 88(7), 2888-92
CODEN: PNASA6; ISSN: 0027-8424
AU Foster, Graham R.; Ackrill, Andrew M.; Goldin, Robert D.; Kerr, Ian M.; Thomas, Howard C.; Stark, George R.
AN 1991:205330 HCAPLUS
DN 114:205330

L66 ANSWER 36 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI X protein of **hepatitis B virus** resembles a serine protease **inhibitor**
SO Jpn. J. Cancer Res. (1990), 81(12), 1191-4
CODEN: JJCREP; ISSN: 0910-5050
AU Takada, Shinako; Koike, Katsuro
AN 1991:138258 HCAPLUS
DN 114:138258

L66 ANSWER 37 OF 37 HCAPLUS COPYRIGHT 2002 ACS
TI trans-Activation of viral enhancers by the hepatitis B virus X protein
SO J. Virol. (1988), 62(2), 427-34
CODEN: JOVIAM; ISSN: 0022-538X
AU Spandau, Dan F.; Lee, Chao Hung
AN 1988:88696 HCAPLUS
DN 108:88696

=> d ab 2,4,5,7,10,25-27,31

L66 ANSWER 2 OF 37 MEDLINE DUPLICATE 1
AB The hepatitis B viral X promoter is known to be positively autoregulated by its own HBx protein, which also interacts with many cellular regulatory proteins. We investigated the effect of activating transcription factor 2 (ATF2) on the activity of the X promoter. Cotransfection of the ATF2 expression vector with a X promoter-chloramphenicol acetyltransferase plasmid repressed the X promoter activity in HepG2 cells. HBx activated activating protein 1 (AP-1)-mediated transcription through the hepatitis B virus E element by 35-fold, while its activation activity was inhibited in the presence of ATF2, suggesting that ATF2 **inhibited** the autoactivation of X promoter by **HBx** and basal transcription mediated by AP-1. Since the binding sites of AP-1 and ATF2 in the hepatitis B virus E element overlap, the repression of X promoter activity by ATF2 is exerted by the competition for the AP-1 binding site and the formation of the ATF2-Jun heterodimer as in the case of the consensus AP-1 element. However, the small X promoter had a ATF2 binding site and was activated by ATF2. These results suggest that the syntheses of X proteins are differentially regulated by ATF2.

L66 ANSWER 4 OF 37 MEDLINE DUPLICATE 3
AB Persistent infection with hepatitis B virus (HBV) is a leading cause of human liver disease and is strongly associated with hepatocellular carcinoma, one of the most prevalent forms of human cancer. Apoptosis (programmed cell death) is an important mediator of chronic liver disease caused by HBV infection. It is demonstrated that the HBV HBx protein acutely sensitizes cells to apoptotic killing when expressed during viral replication in cultured cells and in transfected cells independently of other HBV genes. Cells that were resistant to apoptotic killing by high doses of tumor necrosis factor alpha (TNFalpha), a cytokine associated with liver damage during HBV infection, were made sensitive to very low doses of TNFalpha by HBx. HBx induced apoptosis by prolonged stimulation of N-Myc and the stress-mediated mitogen-activated-protein kinase kinase 1 (MEKK1) pathway but not by up-regulating TNF receptors. Cell killing was blocked by **inhibiting HBx** stimulation of N-Myc or mitogen-activated-protein kinase kinase 1 using dominant-interfering forms or by retargeting HBx from the cytoplasm to the nucleus, which prevents HBx activation of cytoplasmic signal transduction cascades. Treatment of cells with a mitogenic growth factor produced by many virus-induced tumors impaired induction of apoptosis by HBx and TNFalpha. These results indicate that HBx might be involved in HBV pathogenesis (liver disease) during virus infection and that enhanced apoptotic killing by HBx and TNFalpha might select for neoplastic hepatocytes that survive by synthesizing mitogenic growth factors.

L66 ANSWER 5 OF 37 MEDLINE DUPLICATE 4
AB Transactivation of viral and host genes expression by hepatitis B virus X protein (HBx) is believed to be involved in hepatocarcinogenesis. The interaction of **HBx** with the tumor suppressor p53 and its **inhibitory** effect on p53 functions have been reported recently. However, the question of whether p53 is directly involved in HBx transactivation has not yet been addressed. In this study, we delineated the interaction sites of HBx and p53 using far-Western blotting and glutathione S-transferase-resin pull-down assays. The results indicate that the HBx-binding sites are located within the oligomerization and specific DNA-binding domains of p53 and that the p53-binding site was confined to a small region in the HBx transactivation domain. Mutual interference of the transactivations by HBx and p53 was detected by CAT assays in a transient transfection system. Strikingly, transactivation by HBx was observed in the p53-negative cells, Saos-2 and Hep3B, indicating that the transactivation and the p53-**inhibiting** functions of **HBx** are mutually interfering but distinct.

L66 ANSWER 7 OF 37 CANCERLIT
AB We have recently demonstrated that the hepatitis B virus oncoprotein, **HBx**, can bind to the C-terminus of p53 and **inhibits** p53-mediated apoptosis. Here we further examine the physical and functional interactions between HBx and p53. Binding studies using in vitro translated HBx deletion constructs and GST-p53 fusion protein indicate that p53 binds to the distal C-terminus of HBx (between residues 110 and 154). Using a microinjection technique, we show that this same region is necessary for sequestering p53 in the cytoplasm and abrogating p53-mediated apoptosis. While the transactivation domain of HBx also maps to its C-terminus, a comparison of the ability of full-length and truncated HBx to abrogate p53-induced apoptosis vs transactivate SV40- and human nitric oxide synthase-promoter driven reporter constructs suggests that these two functional properties are distinct. Collectively our data indicate that the distal C-terminal domain of HBx, independent of its transactivation activity, complexes with p53 in the cytoplasm preventing its nuclear entry and ability to induce apoptosis.

L66 ANSWER 10 OF 37 CANCERLIT
AB Both human cytomegalovirus (HCMV) and hepatitis B virus (HBV) are known to be etiologically related to liver cirrhosis. Possible interactions between these two oncogenic viruses in liver cells are investigated. Our PCR analyses indicated frequent co-existence of HBV and HCMV-IE2 genomes in the hepatoma cell lines. Cotransfection of IE2- and HBV-expressing plasmids into HepG2 and Huh-7 cells significantly increased the level of HBV large surface and pregenomic/pre-core mRNAs. Promoter-driven CAT assays show that IE2 protein differentially transactivates HBV pre-S, major S and pre-core promoters, but represses the **HBX** promoter. ELISA results show that IE2 protein **inhibits** the secretion of HBs-Ag by increasing cytoplasmic retention, which is likely due to the feedback inhibitory effect of the increased large surface antigens. From preliminary results of studies using a series of deletion/truncation mutants of IE2 protein, it is suggested that different functional domains of IE2 protein are involved in the transactivation and transrepression activities. Possible mediators involved in the transmodulation activity of HCMV-IE2 protein on HBV gene expression are under investigation.

L66 ANSWER 25 OF 37 MEDLINE DUPLICATE 12

L66 ANSWER 26 OF 37 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
AB Structural mutations in the p53 gene of liver tumor (associated with hepatitis B virus (HBV) infections) were studied using a transgenic mouse disease model. Hbx (the HBV gene product) transgenic mice were derived by microinjection of a 1.15 kb HBV subtype adr DNA fragment, which spanned nucleotide positions 707 to 1,756 in the viral genome, into single cell embryos derived from outbred CD1 mice. This segment of DNA contained the entire coding region of the HBx gene and the transcriptional enhancer, the principle RNA start sites, and the polyadenylation site. Tumor development correlated precisely with p53 binding to HBx in the cytoplasms and complete blockage of p53 entry into the nucleus. Analysis of tumor cell DNA showed no evidence for p53 mutation, except in advanced tumors where a small proportion of cells may have acquire specific base mutations. Interferon-alpha **inhibited** **HBx** gene expression in vivo; down-regulation of **HBx** expression in tumor cells resulted in the reentry of p53 into the nucleus, suggesting a possible reversion of the tumor state of growth in these cells. (53 ref)

L66 ANSWER 27 OF 37 MEDLINE DUPLICATE 13
AB Hepatitis B virus produces a small (154-amino acid) transcriptional transactivating protein, HBx, which is required for viral infection and has been implicated in virus-mediated liver oncogenesis. However, the molecular mechanism for HBx activity and its possible influence on cell

proliferation have remained obscure. A number of studies suggest that HBx may stimulate transcription by indirectly activating transcription factors, possibly by influencing cell signaling pathways. We now present biochemical evidence that HBx activates Ras and rapidly induces a cytoplasmic signaling cascade linking Ras, Raf, and mitogen-activated protein kinase (MAP kinase), leading to transcriptional transactivation. HBx strongly elevates levels of GTP-bound Ras, activated and phosphorylated Raf, and tyrosine-phosphorylated and activated MAP kinase. Transactivation of transcription factor AP-1 by **HBx** is blocked by **inhibition** of Ras or Raf activities but not by **inhibition** of Ca(2+)- and diacylglycerol-dependent protein kinase C. **HBx** was also found to stimulate DNA synthesis in serum-starved cells. The hepatitis B virus HBx protein therefore stimulates Ras-GTP complex formation and promotes downstream signaling through Raf and MAP kinases, and may influence cell proliferation.

L66 ANSWER 31 OF 37 CANCERLIT
AB Persistent infection of hepatitis B virus (HBV) raises the risk of occurrence of primary hepatocellular carcinoma (PHC) by two orders. HBx, a protein of 154 amino acid residues encoded by HBV X gene, seems to play oncogenic role since a high incidence of PHC has been reported in HBx transgenic mice. Mutation or deletion of a tumor suppressor gene, p53, has been suspected in HBV-related PHC, but still remains controversial. We asked whether the viral transactivator, HBx, and p53 interact functionally and physically. We examined the effect of p53 on HBx transactivation in a transient expression system using a CAT reporter plasmid which has dimerized 23 bp of HBV enhancer 1 core as enhancer. Mammalian expression plasmids of HBx and wild p53 were introduced together with the CAT reporter into HepG2 cells. The transactivation activity of **HBx** was heavily **inhibited** by p53 in a dose dependent manner. This result suggests that p53 and HBx interfere each other functionally. Then, the possibility of physical interaction of HBx and p53 was examined in vitro by Far-Western blotting using GST-fused protein. The p53 probe could bind HBx but the HBx probe did not bind to p53, suggesting that oligomerized form of p53 is competent to bind to HBx. Delineation of p53 and HBx to define the regions necessary for the interaction is ongoing.

=>
=> s src
FILE 'MEDLINE'
L67 11580 SRC

FILE 'SCISEARCH'
L68 11060 SRC

FILE 'LIFESCI'
L69 4707 SRC

FILE 'BIOTECHDS'
L70 160 SRC

FILE 'BIOSIS'
L71 11441 SRC

FILE 'EMBASE'
L72 8560 SRC

FILE 'HCAPLUS'
L73 11595 SRC

FILE 'NTIS'
L74 1956 SRC

```
FILE 'ESBIOBASE'
L75        5449 SRC

FILE 'BIOTECHNO'
L76        6066 SRC

FILE 'WPIDS'
L77         522 SRC

FILE 'CANCERLIT'
L78        8370 SRC

TOTAL FOR ALL FILES
L79       81466 SRC

=>
=> s activat?
FILE 'MEDLINE'
L80      534689 ACTIVAT?

FILE 'SCISEARCH'
L81      618341 ACTIVAT?

FILE 'LIFESCI'
L82      185669 ACTIVAT?

FILE 'BIOTECHDS'
L83       18088 ACTIVAT?

FILE 'BIOSIS'
L84      597603 ACTIVAT?

FILE 'EMBASE'
L85      504381 ACTIVAT?

FILE 'HCAPLUS'
L86     1006246 ACTIVAT?

FILE 'NTIS'
L87       27088 ACTIVAT?

FILE 'ESBIOBASE'
L88      213397 ACTIVAT?

FILE 'BIOTECHNO'
L89      203645 ACTIVAT?

FILE 'WPIDS'
L90      207925 ACTIVAT?

FILE 'CANCERLIT'
L91      162054 ACTIVAT?

TOTAL FOR ALL FILES
L92     4279126 ACTIVAT?

=> s upstream
FILE 'MEDLINE'
L93       33437 UPSTREAM

FILE 'SCISEARCH'
L94       37258 UPSTREAM

FILE 'LIFESCI'
```

```
L95      23032 UPSTREAM

FILE 'BIOTECHDS'
L96       3232 UPSTREAM

FILE 'BIOSIS'
L97      38010 UPSTREAM

FILE 'EMBASE'
L98      29313 UPSTREAM

FILE 'HCAPLUS'
L99      51073 UPSTREAM

FILE 'NTIS'
L100      5984 UPSTREAM

FILE 'ESBIOBASE'
L101     18965 UPSTREAM

FILE 'BIOTECHNO'
L102     25335 UPSTREAM

FILE 'WPIDS'
L103     53298 UPSTREAM

FILE 'CANCERLIT'
L104     10239 UPSTREAM

TOTAL FOR ALL FILES
L105    329176 UPSTREAM

=> s l79 and l92(5a)l105
FILE 'MEDLINE'
          2313 L80(5A)L93
L106        79 L67 AND L80(5A)L93

FILE 'SCISEARCH'
          2328 L81(5A)L94
L107        78 L68 AND L81(5A)L94

FILE 'LIFESCI'
          1496 L82(5A)L95
L108        31 L69 AND L82(5A)L95

FILE 'BIOTECHDS'
           132 L83(5A)L96
L109         0 L70 AND L83(5A)L96

FILE 'BIOSIS'
          2453 L84(5A)L97
L110        79 L71 AND L84(5A)L97

FILE 'EMBASE'
          1993 L85(5A)L98
L111        60 L72 AND L85(5A)L98

FILE 'HCAPLUS'
          2910 L86(5A)L99
L112        70 L73 AND L86(5A)L99

FILE 'NTIS'
            12 L87(5A)L100
L113         0 L74 AND L87(5A)L100
```

```
FILE 'ESBIOBASE'
          1459 L88(5A)L101
L114        54 L75 AND L88(5A)L101

FILE 'BIOTECHNO'
          1622 L89(5A)L102
L115        45 L76 AND L89(5A)L102

FILE 'WPIDS'
           201 L90(5A)L103
L116         0 L77 AND L90(5A)L103

FILE 'CANCERLIT'
           948 L91(5A)L104
L117        51 L78 AND L91(5A)L104

TOTAL FOR ALL FILES
L118       547 L79 AND L92(5A) L105

=> s l79 and (hbv or hbx)
FILE 'MEDLINE'
         10383 HBV
           271 HBX
L119        12 L67 AND (HBV OR HBX)

FILE 'SCISEARCH'
          8576 HBV
           333 HBX
L120        10 L68 AND (HBV OR HBX)

FILE 'LIFESCI'
          4061 HBV
           173 HBX
L121         7 L69 AND (HBV OR HBX)

FILE 'BIOTECHDS'
           424 HBV
             8 HBX
L122         0 L70 AND (HBV OR HBX)

FILE 'BIOSIS'
         10708 HBV
           303 HBX
L123        13 L71 AND (HBV OR HBX)

FILE 'EMBASE'
          8860 HBV
           235 HBX
L124         8 L72 AND (HBV OR HBX)

FILE 'HCAPLUS'
          5198 HBV
           571 HBX
L125        13 L73 AND (HBV OR HBX)

FILE 'NTIS'
            80 HBV
            26 HBX
L126         0 L74 AND (HBV OR HBX)

FILE 'ESBIOBASE'
          2913 HBV
           162 HBX
```

```
L127         7 L75 AND (HBV OR HBX)

FILE 'BIOTECHNO'
          4475 HBV
           188 HBX
L128         7 L76 AND (HBV OR HBX)

FILE 'WPIDS'
           599 HBV
            11 HBX
L129         3 L77 AND (HBV OR HBX)

FILE 'CANCERLIT'
          3459 HBV
           184 HBX
L130         8 L78 AND (HBV OR HBX)

TOTAL FOR ALL FILES
L131        88 L79 AND (HBV OR HBX)

=> s (l118 or l131) and py=<1998 range=2002,
FILE 'MEDLINE'
'2002,' IS NOT A VALID RANGE FOR FILE 'MEDLINE'
SEARCH ENDED BY USER

FILE 'SCISEARCH'
            49 PY=<1998
L132         0 (L107 OR L120) AND PY=<1998

FILE 'LIFESCI'
           464 PY=<1998
L133         0 (L108 OR L121) AND PY=<1998

FILE 'BIOTECHDS'
            13 PY=<1998
                 (PY=<1998)
L134         0 (L109 OR L122) AND PY=<1998

FILE 'BIOSIS'
         69320 PY=<1998
L135         0 (L110 OR L123) AND PY=<1998

FILE 'EMBASE'
           121 PY=<1998
L136         0 (L111 OR L124) AND PY=<1998

FILE 'HCAPLUS'
          1339 PY=<1998
L137         0 (L112 OR L125) AND PY=<1998

FILE 'NTIS'
          2686 PY=<1998
L138         0 (L113 OR L126) AND PY=<1998

FILE 'ESBIOBASE'
           160 PY=<1998
L139         0 (L114 OR L127) AND PY=<1998

FILE 'BIOTECHNO'
       1165533 PY=<1998
L140        27 (L115 OR L128) AND PY=<1998

FILE 'WPIDS'
          3729 PY=<1998
```

```
                (PY=<1998)
L141         0 (L116 OR L129) AND PY=<1998

FILE 'CANCERLIT'
         35768 PY=<1998
L142         1 (L117 OR L130) AND PY=<1998

TOTAL FOR ALL FILES
L143        28 (L118 OR L131) AND PY=<1998

=> fil medl
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   132.98     133.19

FILE 'MEDLINE' ENTERED AT 11:47:07 ON 04 OCT 2002

 => s (l118 or l131) and py=<1998 range=2002000000,
          6039 PY=<1998
L144         0 (L106 OR L119) AND PY=<1998

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.38     133.57

STN INTERNATIONAL LOGOFF AT 11:47:41 ON 04 OCT 2002
```